Mesenchymal stem cells inhibit multiple myeloma cells via the Fas/Fas ligand pathway.

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Public Summary:
Our finding has opened up a new way of thinking about the effect of mesenchymal stem cells against multiple myelomacells and a new way of moving forward.

Scientific Abstract:
INTRODUCTION: Cell-based therapy represents a new frontier in the treatment of a wide variety of human diseases traditionally associated with morbidity outcomes, including those involving inflammation, autoimmunity, tissue damage, and cancer. However, the use of mesenchymal stem cells (MSCs) to treat multiple myeloma (MM) bone disease has raised concerns. Specifically, evidence has shown that infused MSCs might support tumor growth and metastasis. METHODS: In this study, we used a standard disseminated MM model in mice to identify the in vivo effects of intravenous MSC infusion. In addition, a series of in vitro co-culture assays were preformed to explore whether Fas/Fas ligand (Fas-L) is involved in the inhibitory effects of MSCs on MM cells. RESULTS: In the MM mouse model, treatment of MSCs with highly expressed Fas ligand (Fas-L high MSCs) showed remarkable inhibitory effects on MM indenization in terms of extending the mouse survival rate and inhibiting tumor growth, bone resorption in the lumbus and collum femoris, and MM cell metastasis in the lungs and kidneys. In addition, reduced proliferation and increased apoptosis of MM cells was observed when co-cultured with Fas-L high MSCs in vitro. Furthermore, mechanistically, the binding between Fas and Fas-L significantly induced apoptosis in MM cells, as evidenced through an increase in the expression of apoptosis marker and Fas in MM cells. In contrast, Fas-L null MSCs promote MM growth. CONCLUSIONS: These data suggest that Fas/Fas-L-induced MM apoptosis plays a crucial role in the MSC-based inhibition of MM growth. Although whether MSCs inhibit or promote cancer growth remains controversial, the levels of Fas-L expression in MSCs determine, at least partially, the effects of MSCs on MM cell growth.